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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,847	06/23/2006	Lin Haixiang	NBMP-001	6184

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,847	HAIXIANG, LIN	
	Examiner	Art Unit	
	EMILY M. LE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,31,32,34-38 and 52-78* is/are pending in the application.

4a) Of the above claim(s) *46-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,31,32,34-38 and 52-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/08/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on 11/17/2008 is acknowledged. The traversal is on the ground(s) that Lin et al. failed to evidence that the shared technical feature failed to provide a contribution over the prior art because the composition of Lin et al. does not teach of a composition having the molecular weight/size defined in the claims. This is not found persuasive because contrary to Applicant's assertion, the composition of Lin et al. does encompass the molecular weight/size recited in the claims. The restriction is based on the claims as originally filed. The original claims require that the polynucleotide adjuvant have a molecular weight in the range of 66,000-1200000 Daltons. Lin et al. teaches of a polynucleotide adjuvant having molecular weight of 5-8S. [Page 309, in particular.] This molecular weight is further collaborated by Applicant. Applicant discloses and established that the polynucleotide adjuvant of Lin et al. has a molecular weight in the range of 38,000-107,000 Daltons. Page 7, Table A of Applicant's specification. The molecular weight of the polynucleotide adjuvant of Lin et al. is within the range required by the original claim.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

2. Claims 1-26, 28-30, 33 and 39-45 are cancelled. Claims 52-78 are added. Claims 27, 31-32, 34-38 and 46-78 are pending. Claims 46-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed

the restriction (election) requirement in the reply filed on 11/17/2008. Claims 27, 31-32, 34-38 and 52-78 are under examination.

Interview Summary

3. It should be noted that while the Office notes during the interview that an amendment to the claims would overcome the 102 rejection of the claims as being anticipated by Zong et al. However, contrary to Applicant's assertion, the Office did not state that the rejection of claims as being obvious over Zong et al. and Morahan et al. would be withdrawn. The Office recalls stating that the arguments will be fully considered with Applicant's filed response.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 59, 67 and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 59, 67 and 75, which depend on claims 55, 63 and 71, respectively, recite the limitation "the rabies antigen" in line 1. There is insufficient antecedent basis for this limitation in the claim. For the purpose of examination, the claims are interpreted as reciting a dependency to claims 58, 67 and 74, respectively.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 31-38, 52-54 and 63-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims requires that the polynucleotide adjuvant composition have an average molecular size "equal to" 13.5S and 15 S.

After a careful review of Applicant's disclosure, it is found that written support does not exist for the cited limitation, "equal to" 13.5 S and 15S. Hence, the new matter rejection is appropriate.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 27, 31-32, 34-37 and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zong et al., [1] as evidenced by Lin et al., [2] in view of Morahan et al.

[1] Zong et al. Study on determining the molecular weight of PICKCa and PI,PC with the method of polyacrylamide gel electrophoresis. Chinese Journal of Pharmaceutical Analysis. 1993, Vol. 13, No. 4, pages 219-222. With English abstract, as provided by Applicant on 1/23/2008 IDS.

[2] Lin et al. A new immunostimulatory complex PICKCa in experimental rabies: antiviral and adjvuant effects. Archives of Virology, Vol. 131, Nos: 3-4, September 1993, 307-319. Provided by Applicant on 03/30/2007 IDS.

The claims are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims. Claim 27 requires the size to be in the range of from 13.5 to 24.0 S. Claims 31-32 require the size to be greater than 13.5S and 15 S, respectively. Claim 34, which recites dependency to any one of claims 27 and 31-32, requires the antibiotic to be kanamycin. Claim 35, which recites dependency to any one of claims 27 and 31-32, requires the antibiotic to be kanamycin and the positive ion be calcium. Claim 36, which recites dependency to any one of claims 27 and 31-32, requires the antibiotic to be kanamycin and the source of the positive ion be calcium chloride. Claim 37, which recites dependency to any one of claims 27 and 31-32, requires the antibiotic to be kanamycin sulfate and the positive ion be provided by calcium chloride.

Zong et al. teaches PICKCa. PICKCa is a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, as evidenced by Lin et al. Lin et al. establishes that PIC is polyriboinosinic-polyribocytidylic acid, K is an antibiotic, and Ca is a positive ion. The antibiotic of PICKCa is kanamycin. The positive ion of PICKCa is calcium. The PICKCa of Zong et al. has molecular size ranging from 7.8-13.4S. [Table 2, page 221, in particular.] Regarding claim 36-37, which requires the positive ion be provided by calcium chloride and the antibiotic be kanamycin sulfate, it should be starting material/source does not further limit the claimed invention,

[3] Morahan et al. Antiviral activity and side effects of polyriboinosinic-cytidylic acid complexes as affected by molecular size. Proc. Nat. Acad. Sci., USA, April 1972, Vol. 69, No. 4, 842-846. Provided by Applicant on 12/18/2007 IDS.

particularly since the source does not impart any structural or functional characteristics on the claimed composition.

Zong et al. does not teach of a PICKCa having molecular size range of from 13.5 to 24 S, greater than 13.5 S and 15 S. However, at the time the invention was made, Morahan et al. teaches that the adjuvant activity contributed by PIC correlates with molecular size. Morahan et al. establishes that adjuvant activity increases as molecular size increase. Thus, at the time the invention was made, it would have been prima facie obvious in the art to increase the molecular size of the PICKCa of Zong et al. One of ordinary skill in the art, at the invention was made would have been motivated to do so to optimize the adjuvant activity of PICKCa. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the determination of a workable or optimal range is routinely practiced in the art.

10. Claims 27, 31-32, 38 and 55-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zong et al., in view of Morahan et al., as applied above, in further view of Lin et al.

11. Claim 38, which depends on any one of claims 27 and 31-32, requires that the composition comprise an antigenic compound. Claims 55, 63 and 71 are directed to the composition of claims 38, wherein the molecular size range required by the claims includes greater than 9.3, 13.5 and 12.8-24 S, respectively. Claims 56, 64 and 72, which depend on claims 55, 63 and 71, respectively, recites the limitation of claim 37. Claims 57, 65 and 73, which depend on claims 55, 63 and 71, respectively, requires

that the antigenic compound be a human antigen, a non-human animal antigen, a plant antigen, bacterial antigen, a fungal antigen, a viral antigen, a parasite antigen, or a cancer antigen. Claims 58, 66 and 74, which depend on claims 55, 63 and 71, respectively, require that the viral antigen be rabies antigen. Claims 59, 67 and 75, which is interpreted to depend on claims 58, 66 and 74, respectively, require that the rabies antigen be an inactivated purified rabies antigen. Claims 60, 68 and 76, which is interpreted to depend on claims 55, 63 and 71, respectively, require that the composition be capable of eliciting an enhanced combined specific humoral and/or cell mediated immune response. Claims 61, 69 and 77, which is interpreted to depend on claims 55, 63 and 71, respectively, require that the composition or its components (PICKCa and antigenic compound) be in solid form or liquid form that is a solution or a suspension. Claims 62, 70 and 78, which is interpreted to depend on claims 55, 63 and 71, respectively, require that the composition or its components (PICKCa and antigenic compound) be freeze-dried.

The significance of Zong et al. and Morahan et al. is provided above. Neither teaches the inclusion of an antigenic compound with the adjuvant composition. However, Lin et al. teaches the inclusion of an antigenic compound with the same adjuvant composition of Zong et al., PICKCa. Lin et al. includes antigenic compound of Lin et al. is an inactivated purified rabies antigen. The composition, in liquid form, of Lin et al., which comprises PICKCa and inactivated purified rabies antigen is capable of eliciting an enhanced combined specific humoral and/or cell mediated immune response. Thus, at the time the invention was made, it would have been prima facie

obvious for one of ordinary skill in the art to combine the teachings of the cited references. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to produce a composition for use against rabies infection. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because the inclusion of antigenic compounds with adjuvants is routinely practiced in the art.

Additionally, it is not readily apparent if the composition or any of the components (PICKCa and antigenic compound) rendered obvious by the references are freeze dried. However, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made to freeze dry the composition or any of its components. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to facilitate storage of the composition or its components. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because freeze drying is a technique that is routine practiced in the art.

It is noted that in response to the previous rejection, which includes citation of the Morahan et al. reference, Applicant argues that Morahan et al. does not teach that adjuvant activity increases as molecular size increases.

Applicant's argument has been considered, however, it is not found persuasive. As discussed in the previous and instant rejection, Morahan et al. teaches that the adjuvant activity contributed by PIC correlates with molecular size. See Results and Discussion sections. At the cited passages, Morahan et al. teaches that the ability of

PIC complex, which is the component that is contributes the adjuvant activity of PICKCa, to induce serum interferon, an immune response, and enhance the immune response of mice to sheep erythrocytes decreases with decreasing molecular size. In the instant case, Morahan et al. establishes that adjuvant activity increases as molecular size increase.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. It is noted that in response to the obviousness type non-statutory double patenting rejection, a terminal disclaimer is submitted. However, it should be noted that the disclaimer is not approved on the basis that the attorney is not of record. The Office requests that Applicant resubmit the disclaimer with the signature of an attorney of record. In the instance that the submitted terminal disclaimer is signed by an attorney of record, the Office requests that Applicant also resubmit the terminal disclaimer while noting that the disclaimer is signed by an attorney of record. Thus, until a filed terminal disclaimer is approved, the rejections are maintained on the record.

14. Claims 27, 31-32, 34-38 and 52-78 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/331575. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant patent application are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims.

Claim 1 of the copending patent application is also directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims. However, claim 1 of the copending patent application also requires the composition be in a sustained release formulation.

In the instant case, the sustained release formulation of the composition of claim 1 of the copending patent application is a species of composition claimed in the instant patent application. The species anticipates the genus of composition instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 27, 31-32, 34-38 and 52-78 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/331839. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant patent application are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims.

Claim 1 of the copending patent application is also directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size

specified in the claims. However, claim 1 of the copending patent application also requires the composition be formulated for mucosal administration.

In the instant case, the mucosal formulation of the composition of claim 1 of the copending patent application is a species of composition claimed in the instant patent application. The species anticipates the genus of composition instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 27, 31-32, 34-38 and 52-78 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 9 of copending Application No. 12/160853. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant patent application are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims.

Claim 9 of the copending patent application is also directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims. However, claim 9 of the copending patent application also requires the composition be in a sustained release formulation.

In the instant case, the sustained release formulation of the composition of claim 9 of the copending patent application is a species of composition claimed in the instant patent application. The species anticipates the genus of composition instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 27, 31-32, 34-38 and 52-78 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of copending Application No. 12/160584. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant patent application are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims.

Claim 2 of the copending patent application is also directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims. However, claim 2 of the copending patent application also requires the composition be formulated for mucosal administration.

In the instant case, the mucosal formulation of the composition of claim 2 of the copending patent application is a species of composition claimed in the instant patent application. The species anticipates the genus of composition instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

18. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to EMILY M. LE whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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